

In the Claims:

~~Please cancel claim 1 without prejudice to or disclaimer of the subject matter contained therein.~~

Please add the following new claims:

62. (New) A method for producing a transgenic animal, said method comprising:
(a) modifying the nuclear genome of a somatic cell at an endogenous locus by a genetic targeting event;
(b) transferring the modified nuclear genome of said somatic cell to a recipient cell, thereby producing an animal embryo; and
(c) causing said animal embryo to develop to term, thereby producing a transgenic animal.

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63. (New) The method of claim 62, wherein said transgenic animal is a transgenic sheep, cow, bull, goat, pig, horse, camel, rabbit or rodent.

64. (New) The method of claim 62, wherein said genetic targeting event is mediated by homologous recombination.

65. (New) The method of claim 62, wherein said genetic targeting event results in removal of a gene, modification of a gene, upregulation of a gene, gene replacement or transgene placement.

66. (New) The method of claim 62, wherein said genetic targeting event results in inactivation of a gene.

67. (New) The method of claim 62, wherein said genetic targeting event results in a gene targeted cell clone:randomly targeted cell clone ratio of equal to or greater than 1:100.

68. (New) The method of claim 62, wherein said gene targeting event is carried out at a locus abundantly expressed in said somatic cell.

69. (New) The method of claim 62, wherein said modification comprises placing a gene adjacent to an endogenous promoter in said nuclear genome.

70. (New) The method of claim 62, wherein said modification comprises placing a promoter adjacent to an endogenous gene in said nuclear genome.

71. (New) The method of claim 69 or 70, wherein said promoter is a collagen gene promoter.

72. (New) The method of claim 69 or 70, wherein said promoter is a milk protein gene promoter.

73. (New) The method of claim 69 or 70, wherein said promoter directs abundant expression of at least one gene in fibroblast cells.

74. (New) The method of claim 69 or 70, wherein said endogenous promoter directs abundant expression of at least one gene in endothelial cells.

75. (New) The method of claim 62, wherein said modification comprises placing a marker gene at said endogenous locus in said nuclear genome.

76. (New) The method of claim 75, wherein said marker gene is a gene that confers resistance to a drug.

77. (New) The method of claim 76, wherein said gene that confers resistance to a drug is selected from the group consisting of neomycin, G418, hygromycin, zeocin, blasticidin and histidinol.

78. (New) The method of claim 75, wherein said marker gene is selected from the group consisting of HPRT, gpt, a visible marker gene and a gene that can be detected with a single chain antibody/hapten system.

79. (New) The method of claim 78, wherein said visible marker gene is GFP.

80. (New) The method of claim 62, wherein said modification comprises removing a negatively selectable marker gene.

81. (New) The method of claim 80, wherein said negatively selectable marker gene is a toxin gene.

82. (New) The method of claim 62, wherein said genetic targeting event is mediated by lipofection.

83. (New) The method of claim 62, wherein said genetic targeting event comprises the use of a gene targeting vector, which vector comprises a region of homology to a target locus.

84. (New) The method of claim 83, wherein said region of homology is greater than 7 kb in length.

85. (New) The method of claim 62, wherein said genetic targeting event comprises the use of a gene targeting vector which is in a circular form.

86. (New) The method of claim 62, wherein said somatic cell is a primary somatic cell.

87. (New) The method of claim 62, wherein said somatic cell is an epithelial cell, a fibroblast cell, an endothelial cell or a muscle cell.

88. (New) The method of claim 62, wherein said somatic cell is a G₀ cell.

89. (New) The method of claim 88, wherein said G₀ cell is obtained by serum starvation of a somatic cell.

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90. (New) A method for producing transgenic offspring from a transgenic animal, said method comprising:

- (a) modifying the nuclear genome of a somatic cell at an endogenous locus by a genetic targeting event;
- (b) transferring the modified nuclear genome of said somatic cell to a recipient cell, thereby producing an animal embryo;
- (c) causing said animal embryo to develop to term, thereby producing a transgenic animal; and
- (d) breeding said transgenic animal to produce transgenic offspring from said transgenic animal.
